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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,897	09/22/2006	Peter Wisdom Atadja	33310A	7190

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
RAE, CHARLESWORTH E	

ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,897	ATADJA ET AL.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 10/15/08, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

This action is made final.

Status of the Claims

Claims 1-14 and 21-23 are currently pending in this application.

Claims 21-23 are withdrawn for examination purposes for being directed to non-elected subject matter.

Claims 1-14 are under examination.

Miscellaneous

It is noted that claims "1-9" were inadvertently stated as being withdrawn on page 2 of the Office action, mailed 04/15/08. However, these claims are properly pending as evidence by the rejections listing said claims.

The examiner wishes to thank applicant for pointing out this inadvertent error (see applicant's Response, received 10/15/08, page 11).

Response to applicant's arguments/remarks

Claim Objection

The objection to claim 4 is withdrawn in view of the claim amendment.

Rejection under 101

This rejection is withdrawn in view of the claim amendment.

Rejection under 112, 2nd paragraph

This rejection is withdrawn in view of the claim amendment and applicant's persuasive arguments (see applicant's Response, page 12).

REJECTIONS

LACK OF WRITTEN DESCRIPTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

Claims 1-14 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses chemicals which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 1-14 are directed to encompass undisclosed prodrugs and derivative compounds which only correspond in some undefined way to specifically instantly disclosed chemicals. In particular claim 1 recites the term "prodrug thereof," while claim 3 recites the term "staurosporine derivative." None of the undisclosed compounds meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. The specification provides insufficient written

description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed compounds, analogs, etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood*

v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the disclosed chemically structurally defined chemicals, but not the full breadth of the claim(s) meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

Response to applicant's arguments/remarks

Applicant's argument that the instant disclosure provide adequate support for "stausporine derivatives" because one would readily understand how to prepare a stausporine derivative based on the chemical structure and that a skilled artisan would expect such compounds to possess FLT-3 inhibiting properties is not found to be persuasive for the reasons discussed above. It is further noted that applicant is found to be in possession of the disclosed chemically defined stausporine derivatives. However,

the instant specification only provides general disclosure regarding the genus of "stausporine derivatives" which reasonably encompasses a diverse group of undisclosed compounds. Since the specification do not provide specific disclosure on how to make the undisclosed stausporine derivative compounds, applicant is not found to have been in possession of the genus of "stausprine derivatives" at the time the application was originally filed.

With respect to the term "prodrug thereof" as recited in claim 1, applicant's arguments are not found to persuasive to overcome the rejection for essentially the same reasons as discussed above because instant application only provides a general disclosure for prodrugs, but fails to provide specific disclosure on how to specifically make the undisclosed prodrugs encompassed by the instant claims.

Thus, the rejection is maintained.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-14 are rejected under 103(a) as being unpatentable over Remiszewski et al. (US Patent 6,552,065), in view of Verner et al. (US Patent 7,276,612) and Griffin et al. (US Patent Application Pub. No. 2005/0020570 A1).

Remiszewski et al. teach hydroxamate HDA inhibitor compounds, including applicant's elected compound, possess anti-prolfierative properties and have been studied for their therapeutic effects on cancer cells, (abstract; col. 1, lines 14-40; cols. 24-25, Example P3; see also cols. 115-116, **Compound 200 = applicant's elected HDAI**). Remiszewski et al. teach that there remains a need for an active compound that is suitable for treating tumors, including cancerous tumors, that is highly efficacious and stable (col. 1, lines 14-40). Remiszewksi et al. teach that even though butyric acid and its derivatives, including sodium phenylbutyrate, have been reported to induce apoptosis in vitro in human colon carcinoma, **leukemia** and retinoblastoma cell lines,

these agents are not useful pharmacological agents because they tend to be metabolized rapidly and have a very short half-life in vivo (col. 1, lines 14-40).

Although Remiszewski exemplify applicant's elected HDAI compound species for use in treating leukemia, it does specifically teach AML (= applicant's elected disease species). Further, Remiszewski does not teach the instantly claimed combination of an HDAI (i.e. Compound 200) and an FLT-3 inhibitor (i.e. Midostaurin = applicant's elected FLT-3 inhibitor compound species).

Verner et al. (US Patent 7,276,612) teach that HDAIs are useful for treating various conditions, including AML, and may be co-administered with other therapeutic agents to treat said conditions (col. 49, line 20-35; col. 50, line 62 to col. 51, line 15; and col. 58, line 51 to col. 59, line 10). Verner et al. do not specifically teach the instant claimed combination of a HDAI (e.g. Compound 200) and a FLT-3 inhibitor (e.g. Midostaurin) for treating AML.

Griffin et al. (US Patent Application Pub. No. 2005/0020570 A1) teach that aberrant expression of the FLT3 gene has been documented in both adult and childhood leukemias, including acute myeloid leukemia (AML), AML with trilineage myelodysplasia (AMLUTMDS), acute lymphoblastic leukemia (ALL), and myelodysplastic syndrome (MDS)(para 0252). Griffin et al. teach that Midostaurin (or PKC42) possesses FLT-3 inhibitory properties that render it particularly useful as an inhibitor of FLT-3 receptors and especially in the treatment of leukemias and myelodysplastic syndromes (paras 0232-0235).

It would have been obvious to a person of skill in the art at the time the invention was made to combine the cited references by adding an FLT-3 inhibitor (e.g. Midostaurin) as taught by Griffin et al. to a HDAI (e.g. Compound 200) as taught by Remiszewski for additive effects in treating AML. One would have been motivated to do so because Vernier et al. suggest that HDAIs may be combined with other agents to treat AML and therefore one would have combined an HDAI (e.g. Compound 200) as taught by Remiszewski with another agent such as a FLT-3 inhibitor (e.g. Midostaurin) as taught by Griffin et al. to treat AML since both classes of drugs are used to treat AML as evidenced by the teaching of Vernier et al. and Griffin et al. ((Cf. In re Kerkhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980). Besides, Griffin et al. teach that AML is associated with deregulated FLT-3 and therefore one would expect that the combination of an HDAI (e.g. Compound 200) as taught by Remiszewski with an FLT-3 inhibitor (e.g. Midostaurin) as taught by Griffin et al. would also be effective in treating AML.

It is noted that Compound 200 as taught by Remiszewski is identical to applicant's elected HDAI compound species and reads on claims 1, 7, 8, 9, 10, 11, 12, 13, and 14.

It is noted that Midostaurin as taught by Griffin et al. is identical to applicant's elected FLT-3 inhibitor compound species and reads on claims 1, 3, 4, 5, and 6.

It is noted that Griffiin et al. and Vernier et al. teach AML (= applicant's elected disease species), which reads on claims 1, and 2.

Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

Response to applicant's arguments/remarks

Applicant's argument that the skilled artisan would not have expected that any benefit to be achieved by combining the two distinct instantly claimed classes of drugs or would be have been motivated to combine said classes of drugs is not found to be persuasive for the reasons discussed because it is routine in the oncology arts to combine drugs that exhibit different mechanisms of action and HDAI and FLT-3 inhibitors exhibit different mechanisms of action for additive, if not synergistic, effects. Thus, it is the examiner's position that one skilled in the art would have been motivated to combine the HDAI and FLT-3 inhibitor as taught by the prior art to treat AML for additive, if not synergistic anti-proliferative effects. Thus, the rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

27 December 2008
/C. R./Examiner, Art Unit 1611

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611